REMARKS

Claims 1, 2, 40 and 66-68 are currently pending in the application.

The claims are rejected under 35 U.S.C. § 102(e) as being anticipated.

Rejection under 35 U.S.C. § 102(e) are overcome.

Claims 1, 2, 40, 66-68 are rejected as being anticipated by Gilbert *et al.*, US 6,495,668 B1 ("Gilbert"). Applicant strongly disagrees that Gilbert specifically anticipates the sequences currently claimed. In the current Office Action, the examiner states:

> "...Gilbert teaches functional fragments of zvegf4 such as the growth factor domain, dimers thereof, and a pharmaceutical composition thereof, wherein said polypeptide fragment is from 113 to 138 amino acid residues in length and comprises amino acid residues 258-370. Thus Gilbert teaches a set of 26 fragments with N-terminus starting at position 233 (138 residues in length) to 258 (113 residues in length), as position 370 is the end of the C-terminus of the zvegf4 molecule. As such Gilbert's 26 fragments of zvegf4 encompass SEQ ID NO;4 (residues of 239-370 of SEQ ID NO:2), and the fragment having residues 247-370 of SEQ ID NO:2 of the present invention and therefore, the reference anticipates the present claims...."

Gilbert does not specifically teach an isolated polypeptide consisting of amino acid residues 239-370 (SEQ ID NO:4), 247-370, 247-338, or 339-370 of SEQ ID NO:2 presently claimed in the current application.

Gilbert teaches an isolated polypeptide of at least 15 amino acid residues comprising an epitope bearing portion of a protein of SEQ ID NO:2 (Column 3, lines 33-35). Specific embodiments are residues 19-179, 35-179, 52-179, 19-245, 35-245, 52-245, 19-249, 35-249, 52-249, 19-253, 35-253, 52-253, 19-255, 35-255, 52-255, 19-257, 35-257, 52-257, 19-370, 35-370, 52-370, 180-370, 246-370, 250-370, and 258-370 of Gilbert's SEQ ID NO:2 (Column 3, lines 38-46; Table 1 at Column 10). None of these correspond to the specific fragments of the applicant's invention, amino acid residues 239-370 (SEQ ID NO: 4), 247-370, 247-338, or 339-370 of applicant's SEQ ID NO:2.

Further, Gilbert teaches an isolated polypeptide comprising a sequence of amino acids of the formula $R1_xR2_yR3_z$ with limitations on the values of x, y, and z such that polypeptides taught

by Gilbert are either R1 or R3 or R1R2R3. R1 is a polypeptide at least 70% identical to amino acids 52-179 of Gilbert's SEQ ID NO:2. R1 does not anticipate 239-370 (SEQ ID NO: 4), 247-370, 247-338, or 339-370 of applicant's SEQ ID NO:2.

R3 is a polypeptide at least 70% identical to 258-370 of SEQ ID NO:2. Gilbert does not describe R3 as containing any part of the R2 sequence, they are separate and distinct. The limitation of 70% identical is intended to capture amino acid changes (*i.e.*, up to 30%) within the 258-370 region. Applicant's 239-370 (SEQ ID NO: 4), 247-370 and 247-338 all contain amino acids from Gilbert's R2 domain and therefore are not anticipated by this teaching of Gilbert. Furthermore, applicant's polypeptide 339-370 of SEQ ID NO: 2 is only 27% identical to Gilbert's R3, calculated as defined by Gilbert (Column 12, lines 53-56).

R1-R2-R3 is a polypeptide defined as including three sequences, namely: R1) at least 70% identical to amino acids 52-179 of SEQ ID NO:2; R2) a polypeptide at least 90% identical to amino acids 180-257; and R3) a polypeptide at least 70% identical to 258-370 of SEQ ID NO:2. The sequences of the present invention do not contain an R1 sequence and therefore are not anticipated by Gilbert's R1-R2-R3 polypeptide.

Gilbert does however teach specific sequences that are exceptions to the formula. In the context of functional domains of the protein, Gilbert teaches a growth factor domain that extends from amino acid residues 246-370, 250-370 or 258-360 SEQ ID NO:2 (column 9 lines 39-43 and column 10, Table 1, lines 23-24). Gilbert does not teach the specific polypeptides consisting of 239-370 (SEQ ID NO: 4), 247-370, 247-338, or 339-370 of applicant's SEQ ID NO:2. The growth factor domain of Gilbert is extended from the 258-360 embodiment to start with residue 246 or 250 based upon his teaching of potential cleavage sites at 245 and 249. Neither of these cleavage sites would give rise to Applicant's polypeptides that begin at 239, 247 and 339. Gilbert states that the taught boundaries can vary ± 5 residues and admits they are imprecise. In contrast, applicant has *specific teaching of purified polypeptides* having amino acid residues 247-370, 247-338, and or 339-370.

Applicant teaches specific fragments 247-370, 247-338 and 339-370 in the specification at page 3 line 12, page 13 line 1, Example 12 page 123 line 19. Applicant teaches fragment 239-370 (SEQ ID NO: 4) of SEQ ID NO:2 throughout the specification and most specifically at

page 13, line 10 through page 14, line 40. In Example 12, applicants show purification of intact and cleaved products of the 30664188.m99 protein. Under reducing conditions SDS-PAGE shows three bands of molecular weight 22-25kDa (band I), about 16kDa (band II) and about 5-6kDa (band III). Further, N-terminal amino acid analysis of these fragments determines that band I and II begin at residue 247 and band III begins at residue 339. Hence these bands correspond to fragments having amino acid residues 247-370, (band I), 247-338 (band II) and 339-370 (band III).

The examiner has interpreted the limitation "113 to 138 amino acid residues in length and comprises amino acid residues 258-370 of SEQ ID NO:2..." in Gilbert's claim 1 of to mean:

> "a set of 26 fragments with N-terminus starting at position 233 (138 residues in length) to 258 (113 residues in length), as position 370 is the end of the C-terminus of the zvegf4 molecule".

However it is clear from the specification and the file wrapper of 6,495,668 that what is meant is 113 amino acids which is the length of amino acids 258-370 and, optionally, up to 25 additional residues which include an amino –terminal methionine residue, small linker peptides, affinity tags, and cleavage sites (Column 14, lines 29-40). There are only two polypeptides disclosed by Gilbert in which the 25 additional residues could be interpreted as including certain additional residues from SEQ ID NO:2. These are 246-370 and 250-370 (Column 10, Table 1), neither of which anticipates Applicant's specific polypeptides. Gilbert does not teach the specific polypeptides consisting of 239-370 (SEQ 4), 247-370, 247-338, or 339-370 of applicant's SEQ ID NO:2.

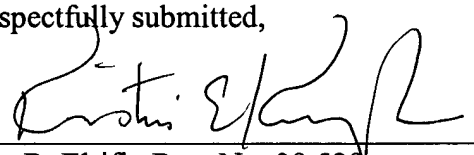
Therefore Applicants request that this rejection be withdrawn.

CONCLUSION

On the basis of the foregoing remarks, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

A petition for a one month extension of time and associated fee under 37 C.F.R. §1.17(a)(1) accompanies this response. The Commissioner is authorized to charge any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 15966-577 (CURA-77).

Respectfully submitted,



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